REMARKS

Claims 1, 8, 10-14, 21, 22, 26-41, and 61-63 were pending in the present application. Claims 10, 29, 30, 36, and 38-41 were withdrawn from consideration and claims 1, 8, 11-14, 21, 22, 26-28, 31-35, 37, and 61-63 are rejected. By virtue of this response, claims 13, 28-31 and 35-41 have been canceled, claims 1, 8, 10-12, 14, 21, 22, 26, 32, 33, 61, and 63 have been amended and new claims 64-66 have been added. Accordingly, claims 1, 8, 10-14, 21, 22, 26, 27, 32-34, and 61-66 are currently under consideration. No new matter has been added by these amendments.

Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of those claims as previously presented. Applicant expressly reserves the right to pursue the prosecution of any presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

I. Claim Amendments

As noted above, claims 1, 8, 10-12, 14, 21, 22, 26, 32, 33, 61, and 63 have been amended. Claims 13, 28-31 and 35-41 have been canceled. New claims 64-66 have been added.

Claim 1 has been amended to include a step of correlating the quantity of the marker to the level of *de novo* fatty acid synthesis in the tissue, and to clarify that the marker of *de novo* fatty acid synthesis is quantified from a fluid sample from an organism, wherein the fluid sample is blood or a blood product. Claim 1 has also been amended to indicate that the marker of fatty acid synthesis comprises (a) palmitoleic acid or the ratio of palmitoleic acid to palmitic acid quantified from the free fatty acid fraction of the blood or blood product, wherein the method is a method to assess *de novo* fatty acid synthesis in adipose tissue; or (b) palmitoleic acid or the ratio of palmitoleic acid to palmitic acid quantified from the phosphatidylcholine or cholesterol ester fraction of the blood or blood product, wherein the method is a method to assess *de novo* fatty acid synthesis in liver tissue. Support for these amendments is found throughout the specification, for example, at lines 5-23 of page 4, and at lines 14-27 of page 15.

Claims 8, 10, 11, 12, 14, 22, 26, and 63 have been amended for consistency with amended claim 1.

Claim 21 has been amended to delete clause (3).

Claims 32 and 33 have been amended due to the cancellation of claim 28.

An apparent typographical error has been corrected in amended claim 61.

New claim 64 finds support in the specification, for example, at lines 6-10 of page 29. New claim 65 finds support in the specification, for example, at lines 10-14 of page 29. New claim 66 finds support in the specification, for example, at lines 7-10 of page 16.

No new matter is added by the claim amendments.

II. Claim Rejections under 35 U.S.C. § 112, first paragraph (enablement)

The Office has rejected claims 1, 8, 11-14, 21, 22, 26-28, 31-35, 37, and 61-63 under 35 U.S.C. § 112, first paragraph, because the specification allegedly "does not reasonably provide enablement for assessing *de novo* fatty acid synthesis in a liver tissue (elected species) by quantifying a marker in the cholesterol ester fraction of blood. In addition, the specification does not provide for a correlation with any disease state or propensity for weight gain or compatibility, etc." Office Action, at page 2.

Applicant respectfully disagrees and traverses this rejection.

Without acquiescing to the merits of the rejection, and solely to expedite prosecution, applicant has amended claim 1 without prejudice. Claim 1 as amended is now directed to a method of assessing *de novo* fatty acid synthesis in a tissue of an organism, comprising quantifying a marker of *de novo* fatty acid synthesis in a fluid sample from the organism, and correlating the quantity of the marker to the level of *de novo* fatty acid synthesis in the tissue, wherein the fluid sample is blood or a blood product, and wherein the marker of *de novo* fatty acid synthesis comprises: (a)

palmitoleic acid or the ratio of palmitoleic acid to palmitic acid quantified from the free fatty acid fraction of the blood or blood product, wherein the method is a method to assess *de novo* fatty acid synthesis in adipose tissue; or (b) palmitoleic acid or the ratio of palmitoleic acid to palmitic acid quantified from the phosphatidylcholine or cholesterol ester fraction of the blood or blood product, wherein the method is a method to assess *de novo* fatty acid synthesis in liver tissue. Rejected claims 8, 10-14, 21, 22, 26, 27, 32-34 and 61-63 all depend directly or indirectly from claim 1 and therefore incorporate all elements of claim 1. 35 U.S.C. § 112, fourth paragraph (West 2008).

The Office asserts that the claimed method "fails to state how the 'quantifying' leads to or is correlated with the 'assessing' which is required by the preamble" of the claim. Office Action, at page 7. Applicant respectfully submits that the added step of "correlating the quantity of the marker to the level of *de novo* fatty acid synthesis in the tissue" in claim 1 renders moot this aspect of the rejection and asks that it be withdrawn.

Without acquiescing to the merits of the rejection, and solely to expedite prosecution, applicant has canceled claims 13, 28-31 and 35-41 without prejudice. The cancellation of claims 13, 28-31 and 35-41 renders moot the rejection of those claims under 35 U.S.C. § 112, first paragraph. Because canceled claims 13, 28-31 and 35-41 were directed to aspects of the invention relating to the correlation of *de novo* fatty acid synthesis with propensity for weight gain, weight loss, or obesity, those amendments also render moot the Office's arguments regarding several references purportedly showing that "the state of the art with regard to a correlation between a weight gain or loss due to a nutritional treatment and a change in a marker of *de novo* fatty acid synthesis in a tissue . . . is undeveloped." Office Action, at page 4. Therefore, applicant will not address those arguments herein.

The Office stated that "[p]latelets, red [blood] cells, leukocytes are all blood products" and asserted that "one would not reasonably assume that *de novo* fatty acid synthesis in the liver could be assessed by sampling the fatty acid content of platelets, nor does the specification teach such relationships." Office Action, at page 3. Applicant respectfully asserts that one skilled in the art would recognize that the markers of *de novo* fatty acid synthesis would not be quantified from a

cellular component of a blood product, *i.e.*, a purified platelet, red blood cell or lymphocyte fraction. Nevertheless, without acquiescing to the merits of the rejection, and solely to expedite prosecution, applicant has amended claims 1, 8, 12, 14, 22 and 26 to clarify that a marker of *de novo* fatty acid synthesis is quantified from a fluid sample from an organism, and that the fluid sample is blood or a blood product. Thus, the claims as amended encompass quantifying markers of *de novo* fatty acid synthesis from plasma, serum, and/or any lipoprotein fractions isolated from plasma or serum. Applicant respectfully submits that those amendments render this aspect of the rejection moot, and ask that it be withdrawn.

A. The Specification Provides Support for Enablement of the Full Scope of the Claims.

Applicant respectfully contends that the claims as amended are fully enabled, and that the specification enables one of ordinary skill in the art to make and use the full scope of the claimed invention without undue experimentation. The disclosures in the specification illustrate that, contrary to the Office's assertions, there is a correlation between (1) the quantity of palmitoleic acid (16:1n7) and/or the ratio of palmitoleic acid (16:1n7) to palmitic acid (16:0) quantified from the free fatty acid fraction of blood or a blood product or from the phosphatidylcholine or cholesterol ester fraction of blood or a blood product and (2) *de novo* fatty acid synthesis in adipose or liver tissue. Those experiments clearly indicate that the quantity of palmitoleic acid (16:1n7) and/or the ratio of palmitoleic acid (16:1n7) to palmitic acid (16:0) in the free fatty acid fraction of blood or a blood product and in the phosphatidylcholine or cholesterol ester fractions of blood or a blood product can be used as markers to assess *de novo* fatty acid synthesis in adipose or liver tissue. Thus, Applicant respectfully asserts that the claims as amended are fully enabled by the disclosures of the specification.

The Office asserts that the specification "fails to correlate any of the claimed, broad classifications with a consistent variation in cholesterol ester palmitate or palmitoleate from plasma with *de novo* fatty acid synthesis changes in the liver." Office Action, at page 3. Applicants respectfully submit that, contrary to the Office's assertions, Example 1 at pages 38-62 of the

specification provides data (in Tables 5-8) demonstrating a correlation between (a) the quantity of palmitoleic acid (16:1n7) and the ratio of palmitoleic acid (16:1n7) to palmitic acid (16:0) in the free fatty acid fraction of blood or a blood product and in the phosphatidylcholine or cholesterol ester fractions of blood or a blood product and (b) *de novo* fatty acid synthesis in adipose or liver tissue.

Example 1 reports the results of a study measuring the concentrations of lipid metabolites present in adipose, plasma, heart and liver tissues in: (1) prediabetic mice (a cross between NZO and NON mouse strains) treated with rosiglitazone (a thiazolidinedione); (2) inbred NON mice treated with CL316,243 (a β-3 adrenergic antagonist); and (3) in control prediabetic and inbred NON mice.

Applicant respectfully asserts that thiazolidinedione compounds, a class of compounds which includes rosiglitazone, were known in the art to increase *de novo* fatty acid synthesis in the liver. CL316,243, on the other hand, has been linked to decreased lipogenesis. *See, e.g.*, Ferrand et al., *J. Physiol. Biochem.* 62(2):89-99, 2006 (previously made of record).

The Office contends that applicant has not provided evidence that it was known at the time of filing that administration of rosiglitazone increased *de novo* fatty acid synthesis. Applicant respectfully refers the Office to an article by Oakes et al., entitled "The insulin sensitizer, BRL 49653, reduces systemic fatty acid supply and utilitzation and tissue lipid availability in the rat." *See, e.g.*, Oakes, N.D., et al., *Metabolism* 46(8):935-942, August 1997 (listed on the Supplemental Information Disclosure Statement submitted herewith). In 1997, Oakes and colleagues showed that rats fed both high-fat and high-starch diets and treated with BRL 49653, a thiazolidinedione compound, displayed increased glucose incorporation into fatty acid (*i.e.*, *de novo* fatty acid synthesis). *See, e.g.*, Oakes et al., at page 938. Rosiglitazone is also a thiazolidinedione. Furthermore, Oakes reported that the observed effects of BRL 49653 on glucose and/or lipid metabolism "appear to be generally conserved for this class of compounds," though individual thiazolidinedione compounds may differ in potency. *Id.* at pages 939-40. Applicant respectfully submits that the Oakes article shows it was known in the art at or before the time of filing that

administration of thiazolidinedione compounds, such as rosiglitazone, increased *de novo* fatty acid synthesis.

The results of the study in Example 1 are shown in Tables 5-8 and described on pages 60-62 of the specification. The lipid composition data in Tables 5-6 at pages 46-47 and 49-50 of the specification shows that when rosiglitazone (*i.e.*, a thiazolidinedione, a class of compounds known to increase *de novo* fatty acid synthesis) was given to the prediabetic mice, the amount of palmitoleic acid in cholesterol esters in plasma, the amount of palmitoleic acid in phosphatidylcholines in plasma, and the amount of palmitoleic acid in free fatty acids in plasma all increased relative to control. The data in Tables 5-6 at pages 46-47 and 49-50 of the specification also show that when rosiglitazone was given to the prediabetic mice, the ratio of palmitoleic acid to palmitic acid in cholesterol esters in plasma, the ratio of palmitoleic acid to palmitic acid in phosphatidylcholines in plasma, and the ratio of palmitoleic acid to palmitic acid in free fatty acids in plasma all increased relative to control.

Moreover, Example 1 also shows at page 61, lines 14-16, that treatment of mice with CL316,243, a β-3 adrenergic antagonist, induced a substantial decrease in palmitoleic acid concentrations in most lipid classes in heart, liver, adipose, and plasma. The lipid composition data in Tables 7 and 8 at pages 52, and 58-59 of the specification shows that when CL316,243 was given to the mice, the amount of palmitoleic acid, as well as the ratio of palmitoleic acid to palmitic acid decreased in phosphatidylcholines in plasma, free fatty acids in plasma, and cholesterol esters in plasma relative to the controls.

With respect to the results shown for mice treated with CL316,243, the Office states "[t]he *de novo* fatty acid synthesis in the liver, at least from an analysis of total fatty acid content, appears to be unaffected. Since experimental mice have tightly controlled diets and should have been paired fed for the experiments since the effect of diet on lipid content of the animal is well known, variation of total fatty acid content from the control to experimental should be some sort of measure of *de novo* synthesis." Office Action, at page 4. First, applicant notes that it is variation in the quantity of particular fatty acids themselves, not the total fat content that indicates modulation of *de*

novo fatty acid synthesis. *See, e.g.*, Specification, at lines 6-13 of page 34. Furthermore, the Examiner has provided no citation that would suggest that total fat content in the liver would be an accurate reflection of hepatic fat synthesis and has no means of assessing how major factors that could affect total fat content in the liver (*e.g.*, dietary intake, metabolic rate, cholesterol synthesis and bile acid secretions rates) were affected by the treatment of the mice with the drug. Thus, the Examiner has not provided adequate support for her assertion that *de novo* fatty acid synthesis is unaffected by CL316,243. As noted above, CL316,243 has been shown to be linked to decreased lipogenesis. *See, e.g.*, Ferrand et al., *J. Physiol. Biochem.* 62(2):89-99, 2006.

Thus, Applicant has demonstrated in Example 1 of the specification that both palmitoleic acid and the ratio of palmitoleic acid to palmitic acid in the free fatty acid fraction of plasma and in the phosphatidylcholine and cholesterol ester fractions of plasma positively correlate with rosiglitazone treatment, which in turn, positively correlates with *de novo* fatty acid synthesis in both adipose and the liver. The experiments described in Example 1 also demonstrate that a decrease in the level of palmitoleic acid or in the ratio of palmitoleic acid to palmitic acid in the free fatty acid fraction of plasma and in the phosphatidylcholine and cholesterol ester fractions in plasma correlate with CL316,243 treatment, which in turn, correlates with decreased *de novo* fatty acid synthesis. These data support Applicant's claim that both palmitoleic acid and the ratio of palmitoleic acid to palmitic acid in the free fatty acid, phosphatidylcholine, and cholesterol ester fractions in plasma can be used as markers for *de novo* fatty acid synthesis in adipose and the liver.

B. The Declaration from Steven M. Watkins Provides further Support for Enablement of the Full Scope of the Claims.

Applicant also submitted a Declaration from Steven M. Watkins (the "Watkins Declaration"), filed with the Amendment in Response to Non-Final Office Action of June 27, 2007, presenting data from four additional studies (Studies A-D) further confirming that palmitoleic acid and the ratio of palmitoleic acid to palmitic acid in cholesterol esters in plasma or serum can serve as markers of *de novo* fatty synthesis in liver. The results of Study A demonstrate the positive correlation of both (a) palmitoleic acid in cholesterol esters (CE16:1n7) and (b) the ratio of

palmitoleic acid to palmitic acid in cholesterol esters (CE16:1n7/CE16:0) in blood to the expression of fatty acid synthase (FAS) in the liver. Study B showed that CE16:1n7 and the ratio of CE16:1n7/CE16:0 positively correlated with weight gain induced by treatment with a thiazolidinedione PPARγ agonist. Study C provided data showing that increased levels of CE16:1n7 and CE16:1n7/CE16:0 positively correlated with rosiglitazone treatment in humans. Finally, Study D, showed that serum levels of CE16:1n7 and CE16:1n7/CE16:0, markers which correlate with *de novo* fatty acid synthesis, were reduced during caloric restriction and weight loss.

The Office asserts that the data presented in Study A and Exhibit 2 of the Watkins Declaration demonstrated that "elevated CE16:1n7 and the ratio of CE16:1n7/CE16:0 is correlated with rosiglitazone administration to *db/db* mice," but failed to demonstrate that the markers of *de novo* fatty acid synthesis correlated with fatty acid synthase ("FAS") expression. Office Action, at page 8. Applicant respectfully traverses.

Study A compared the level of palmitoleic acid in cholesterol esters (CE16:1n7) or the ratio of palmitoleic acid to palmitic acid in cholesterol esters (CE16:1n7/CE16:0) in normal (*db/+*) or leptin-receptor deficient (*db/db*) mice treated with increasing concentrations of rosiglitazone or vehicle alone to the level of fatty acid synthase ("FAS") expression measured by quantitative reverse transcriptase-polymerase chain reaction ("RT-PCR"). The data presented in Exhibit 2 of the Watkins Declaration clearly shows that the level of CE16:1n7 and the ratio of CE16:1n/CE16:0 positively correlate with expression of FAS in rosiglitazone-treated, leptin receptor-deficient (*db/db*) mice. That result was confirmed by statistical analysis represented by the "r" and "p" values included under the legend "FAS Expression" on both graphs. The "r" value is the "Pearson's Correlation Coefficient," a standard statistical method known in the art which measures the strength of the correlation between two variables. In this case, the "r" value measures the strength of the correlation between FAS expression and the level of CE16:1n7 (left panel of Exhibit 2) and between FAS expression and the ratio of CE16:1n7/CE16:0 (right panel of Exhibit 2). A positive Pearson's Correlation Coefficient between 0.7 and 1.0 indicates a strong positive correlation between the two measured variables. The "p" value measures the likelihood that a particular "r" value occurred by

chance. A low "p" value indicates the likelihood that a particular positive correlation is not random. Thus, the data in Exhibit 2 of the Watkins Declaration indicates that FAS expression shows a strong positive correlation with both CE16:1n7 levels and the ratio of CE16:1n7/CE16:0, and that the correlation is statistically significant.

The Office asserts that the data presented in Study B and Exhibit 3 of the Watkins Declaration demonstrated at best "that Zucker diabetic rats all gained weight over the course of the experiment." Office Action, at page 8. Applicant respectfully traverses.

Study B compared the level of CE16:1n7 or the ratio of CE16:1n7/CE16:0 to body weight gain in mice treated with a PPARα agonist, a PPARδ agonist, a PPARγ agonist (not rosiglitazone), and vehicle alone. Only PPARγ agonists have been shown to correlate with increased *de novo* fatty acid synthesis. Study B used juvenile animals that continued to grow over the course of the experiment, so the data presented in Exhibit 3 of the Watkins Declaration represents relative weight gain among all animals. As expected, mice treated with a PPARγ agonist gained significantly more weight than mice treated with a PPARα agonist, a PPARδ agonist, or vehicle alone. Furthermore, that weight gain correlated positively with the level of CE16:1n7 (left panel in Exhibit 3) or the ratio of CE16:1n7/CE16:0 (right panel in Exhibit 3). That result was also confirmed by statistical analysis represented by the "r" and "p" values included under the legend "Body Weight Gain" on both graphs. As discussed above, a positive Pearson's Correlation Coefficient between 0.7 and 1.0 indicates a strong positive correlation between two measured variables. A low "p" value indicates the likelihood that a particular positive correlation did not occur by chance. Thus, the data in Exhibit 3 of the Watkins Declaration indicates that body weight gain in mice treated with a PPARγ agonist known to correlate with increased *de novo* fatty acid synthesis shows a strong positive correlation with both CE16:1n7 levels and the ratio of CE16:1n7/CE16:0, and that the correlation is statistically significant.

The Office asserts that "[n]o correlation is seen between weight increases in the control (not administered rosiglitazone) and CE16:1n7 levels" in Study C and Exhibit 4 of the Watkins

Declaration. Office Action, at page 9. Applicant notes that no correlation was seen between weight increases and CE16:1n7 levels in the control population because weight gain data was not obtained for Study C. *See, e.g.*, Watkins Declaration, at page 6, paragraph 21. In Study C, diabetic patients were treated with rosiglitazone, metformin, glyburide, or placebo for a period of four weeks. Neither metformin nor glyburide are PPARγ agonists. The concentration of various lipid metabolites were measured in serum, muscle, and adipose at baseline, two weeks post-treatment, and four weeks post-treatment. Because no significant changes were observed in the metformin, glyburide, or placebo groups, Exhibit 4 presented only the level of CE16:1n7 (left panel in Exhibit 4) or the ratio of CE16:1n7/CE16:0 (right panel in Exhibit 4) from the rosiglitazone-treated patients. This experiment showed that patients treated with rosiglitazone, a drug known to increase levels of *de novo* fatty acid synthesis, displayed elevated levels of CE16:1n7 and elevated ratios of CE16:1n7/CE16:0.

Finally, with respect to Study D of the Watkins Declaration, the Office noted that:

> [i]t is difficult to understand how this study is related to the claimed methods because the example is not related to the propensity, risk or metabolic basis for obesity. Nor is the example related to lipogenesis since at page 31 of the specification, it is stated that fasting increases de novo lipogenesis in the liver. However, according to Study D, CE16:1n7 levels are decreased.

Office Action, at page 9. First, applicant respectfully notes that severe caloric restriction and fasting are different nutritional interventions: fasting subjects receive no food whatsoever, while subjects on severe caloric restriction receive a carefully measured amount of calories each day. Second, the Office correctly observed that Study D is not related to lipogenesis. Instead, Study D shows the effect of severe caloric restriction on *de novo* fatty acid synthesis, examining its effect on body weight and levels of CE16:1n7 and the ratio of CE16:1n7/CE16:0. The data presented in Exhibit 5 of the Watkins Declaration shows that both levels of CE16:1n7 and the ratio of CE16:1n7/CE16:0 decreased in subjects under severe caloric restriction. Such subjects would be expected to have decreased levels of *de novo* fatty acid synthesis in times of energy deficit, because *de novo* fatty

acid synthesis is a typical metabolic response to the presence of an energy surplus, not an energy deficit. Specification, at lines 12-14, on page 31.

C. The Claimed Methods are Patentable Subject Matter under Current Federal Circuit Precedent in Metabolite Laboratories Inc.

The Office stated that "[c]orrelating or assessing to be mental steps. It is noted that the claim has only one active step, quantifying." Office Action, at page 6. The Office directed applicant to the Supreme Court's opinion in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 79 U.S.P.Q.2d 1065 (Supreme Court, June 22, 2006), and the pending Federal Circuit case *Classen Immunotherapies v. Biogen* (Appeal No. 06-1634), alleging that "the fact patterns are similar" to the instant case. Office Action, at page 6. While the Office acknowledged that "no final legal determination has yet been made whether or not such methods are eligible subject matter under § 101, these cases are brought to applicants' attention in order to promote a more positive and robust claim." Office Action, at page 7.

Applicant acknowledges that to certain readers, those cases may appear to share some similarity in fact patterns. In response, however, Applicant respectfully asserts that the Supreme Court revoked its initial grant of certiorari in *Laboratory Corp. of America* and the Federal Circuit has yet to issue an opinion in *Classen Immunotherapies*. Thus, the Federal Circuit's holding in *Metabolite Laboratories, Inc.* remains good law. In that case, the Federal Circuit held valid and infringed a method claim comprising the steps of (1) assaying a body fluid for an elevated level of total homocysteine; and (2) correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate. *Metabolite Laboratories Inc. v. Laboratory Corp. of America Holdings*, 71 U.S.P.Q.2d 1081, 1083-84 (Fed. Cir. 2004).

The Office further asserts that, in *Metabolite Laboratories Inc.*, the Federal Circuit concluded that "claims to methods of assaying or diagnosing require a 'correlating' step in which a particular test result is correlated **unambiguously** with a particular conclusion." Office Action, at page 7 (citing *Metabolite Laboratories Inc.*, 71 U.S.P.Q.2d at 1088) (emphasis original). Applicant

respectfully asserts that the Federal Circuit did not reach such a conclusion. Instead, the court simply refused to read an additional limitation into the claim further requiring a confirmatory step linking a deficiency of cobalamin or folate to diagnosed clinical symptoms. *Metabolite Laboratories Inc.*, at 1088. Thus, contrary to the Office's position, applicant need not correlate the quantity of a marker of *de novo* fatty acid synthesis "unambiguously with a particular conclusion" to satisfy the enablement requirement. A reasonable correlation with the scope of the claims is all that is required. MPEP § 2164.08, at page 2100-210 (noting that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims")(citing *In re Fisher*, 427 F.2d 833, 839 (CCPA 1970). Applicant respectfully submits that the specification and additional data from the Watkins Declaration filed with the Amendment in Response to Non-Final Office Action of June 27, 2007, clearly satisfy that standard.

Applicant contends that the specification *does* demonstrate that there is a correlation between (a) palmitoleic acid (16:1n7) and the ratio of palmitoleic acid (16:1n7) to palmitic acid (16:0) in the free fatty acid fraction of blood or a blood product, or from the phosphatidylcholine or cholesterol ester fractions of blood or a blood product and (b) *de novo* fatty acid synthesis in adipose or liver tissue. Moreover, the disclosures of the specification are further bolstered by the additional data provided in the Watkins Declaration. Accordingly, Applicant respectfully submits that the claims, as amended, are enabled for their full scope.

In light of the claim amendments, the remarks above, and the previously submitted Watkins Declaration, applicant respectfully asks the Office to withdraw the rejection of claims 1, 8, 11-14, 21, 22, 26-28, 31-35, 37, and 61-62 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, Applicant respectfully asks the Examiner to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 475512000400. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 14, 2008

Respectfully submitted,

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